

**WHAT IS CLAIMED:**

1. A binding motif of a receptor capable of binding a cytoplasmic protein, said binding motif comprising an amino acid sequence wherein at least one amino  
5 acid is serine/threonine.

2. A binding motif according to claim 1 wherein the serine/threonine residue corresponds to a serine residue at position 585 of the common  $\beta_c$  according to Figure 1.  
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3. A binding motif according to claim 1 wherein at least two (2) amino acids are serine.

4. A binding motif according to claim 1 wherein the amino acid sequence  
15 includes the sequence

-S-X-S/T-

wherein the X is any amino acid.

5. A binding motif according to any claim 1 further including flanking amino  
20 acids selected from R and X-P wherein X is any amino acid such that the flanking amino acids individually or co-operatively contribute to the binding motif for binding to a cytoplasmic protein.

6. A binding motif according to claim 1 wherein the amino acid sequence of  
25 the binding motif includes the sequence:

-R-S-X-S/T-X-P-

wherein X is any amino acid.

7. A binding motif according to claim 1 wherein the the receptor is selected  
30 from the group including:

- (1) GM-CSF/IL-3/IL-5 receptor
- (2) IL6 human interleukin-6 receptor beta chain precursor (IL-6R-beta)
- (3) LEPR human leptin receptor precursor (LEP-R) (OB RECEPTOR) (OB-R).

- (4) TNR2 human tumor necrosis factor receptor 2 precursor (tumor necrosis factor)
- (5) VGR1 human vascular endothelial growth factor receptor 1 precursor
- (6) TRK3 human receptor protein-tyrosine kinase TKT precursor (EC 2.7.1.112)
- 5 (7) Q01974 protein-tyrosine kinase transmembrane receptor ROR2 precursor
- (8) FGR1 human basic fibroblast growth factor receptor 1 precursor (BFGF-R)
- (9) Q15426 protein-tyrosine phosphatase, receptor-type, H precursor (EC 3.1.3.48)
- 10 (10) PTPM human protein-tyrosine phosphatase mu precursor (EC 3.1.3.48) (R-PTP-MU).
- (11) PDGS human alpha platelet-derived growth factor receptor precursor (EC 2.7.1.112)
- (12) FGR4 human fibroblast growth factor receptor 4 precursor (FGFR-4) (EC 2.7.1.112)
- 15 (13) FGR2 human fibroblast growth factor receptor 2 precursor (FGFR-2) (EC 2.7.1.112)
- (14) Q13635 patched protein homolog (PTC)
- (15) MANR human macrophage mannose receptor precursor.
- 20 (16) LRP2 human low-density lipoprotein receptor-related protein 2 precursor (megalin)
- (17) IDD human integral membrane protein dgcr2/idd precursor (KIAA0163)
- (18) AMFR human autocrine motility factor receptor precursor (AMF receptor) (gp78)
- 25 (19) ACH5 human neuronal acetylcholine receptor protein, alpha-5 chain precursor.
- (20) KKIT human: stem cell growth factor receptor (proto-oncogene tyrosine-protein kinase kit) (C-KIT) (CD117 antigen)
- (21) TPOR human: thrombopoietin receptor precursor (TPO-R) (myeloproliferative leukemia protein (C-MPL). TPOR or MPL.
- 30 (22) TPOR mouse: thrombopoietin receptor precursor (TPO-R) (myeloproliferative leukemia protein) (C-MPL). TPOR or MPL.

8. A binding motif according to claim 1 wherein the amino acid sequence is selected from the group including:

- |    |         |         |
|----|---------|---------|
|    | (i)     | HSRSLP  |
|    | (ii)    | SSSRP   |
| 5  | (iii)   | SNSKP   |
|    | (iv)    | SDSSP   |
|    | (v)     | SISAP   |
|    | (vi)    | SLSLP   |
|    | (vii)   | SASTP   |
| 10 | (viii)  | SPSFP   |
|    | (ix)    | SNSQP   |
|    | (x)     | SVSSP   |
|    | (xi)    | STSVP   |
|    | (xii)   | SKSPP   |
| 15 | (xiii)  | SRSQP   |
|    | (xiv)   | SSSLP   |
|    | (xv)    | SSSGP   |
|    | (xvi)   | SSSFP   |
|    | (xvii)  | SPSYP   |
| 20 | (xviii) | SGSLP   |
|    | (xix)   | SQSSP   |
|    | (xx)    | SPSLP   |
|    | (xxi)   | SGSTP   |
|    | (xxii)  | SVSPP   |
| 25 | (xxiii) | SGSGP   |
|    | (xxiv)  | SLGSSP  |
|    | (xxv)   | SSSQP   |
|    | (xxvi)  | KSSERTP |
|    | (xxvii) | KSSESTP |

30 or a functional equivalent or analogue thereof.

9. A binding motif according to claim 1 wherein the receptor is the GM-CSF/IL-3/IL-5 receptor and comprises a sequence which includes amino acids

HSRSLP corresponding to amino acids 582 to 587 of the common  $\beta_c$  according to Figure 1, a functional equivalent or analogue thereof.

10. A binding motif according to claim 1 wherein the motif corresponds any  
5 one of the following:

Stem Cell Growth Factor Receptor (C-Kit) (Proto-Oncogene Tyrosine- Protein Kinase Kit) (C-KIT) (CD 117 Antigen), including amino acids 863 to 869 according to Figure 2 or amino acid residues 965 to 969 according to Figure 2 or a  
10 functional equivalent or analogue thereof;

Thrombopoietin Receptor Precursor (TPO-R) (Myeloproliferative Leukemia Protein) (C-MPL), (TPOR or MPL) including amino acids 573 to 579 according to Figure 3 or a functional equivalent or analogue thereof;

15 Thrombopoietin Receptor Precursor (TPO-R) (Myeloproliferative Leukemia Protein) (C-MPL), (TPOR or MPL) including amino acids 564 to 570 according to Figure 4 or a functional equivalent or analogue thereof;

20 IL6B HUMAN interleukin-6 receptor beta chain precursor (IL-6R-BETA), including amino acids 735- 739 having the sequence SSSRP or a functional equivalent or analogue thereof;

LEPR HUMAN leptin receptor precursor (LEP-R) (OB receptor) (OB-R), including  
25 amino acids 991- 995 having the sequence SNSKP or a functional equivalent or analogue thereof;

TNR2 HUMAN tumor necrosis factor receptor 2 precursor (tumor necrosis factor) including amino acids 368- 372 having the sequence SDSSP or a functional  
30 equivalent or analogue thereof;

VGR1 HUMAN vascular endothelial growth factor receptor 1 precursor, including amino acids 1197- 1201 having the sequence SISAP or a functional equivalent or analogue thereof;

TRK3 HUMAN receptor protein-tyrosine kinase TKT precursor (EC 2.7.1.112), including amino acids 444- 448, having the sequence SLSLP or a functional equivalent or analogue thereof;

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Q01974 protein-tyrosine kinase transmembrane receptor ROR2 precursor, including amino acids 435- 439, having the sequence SASTP or a functional equivalent or analogue thereof;

10 FGR1 HUMAN basic fibroblast growth factor receptor 1 precursor (BFGF-R), including amino acids 777- 781, having the sequence SPSFP or a functional equivalent or analogue thereof;

15 Q15426 protein-tyrosine phosphatase, receptor-type, H precursor (EC 3.1.3.48), including amino acids 1082- 1086, having the sequence SNSQP or a functional equivalent or analogue thereof;

20 PTPM HUMAN protein-tyrosine phosphatase MU precursor (EC 3.1.3.48) (R-PTP-MU), including amino acids 818- 822, 833- 837, 1082- 1086 having the sequences SVSSP, STSVP, SKSPP or functional equivalents or analogues thereof;

25 PGDS HUMAN alpha platelet-derived growth factor receptor precursor (EC 2.7.1.112), including amino acids 616- 620 having the sequence SRSQP or a functional equivalent or analogue thereof;

FGR4 HUMAN fibroblast growth factor receptor 4 precursor (FGFR-4) (EC 2.7.1.112), including amino acids 439- 443, 791- 795 having the sequences SSSGP, SSSFP or functional equivalents or analogues thereof;

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FGR2 HUMAN fibroblast growth factor receptor 2 precursor (FGFR-2) (EC 2.7.1.112), including amino acids 780- 784 having the sequence SPSYP or a functional equivalent or analogue thereof;

Q13635 patched protein homolog (PTC), including amino acids 1290- 1294 having the sequence SGSLP or a functional equivalent or analogue thereof;

MANR HUMAN macrophage mannose receptor precursor, including amino acids  
5 1432- 1436 having the sequence SQSSP or a functional equivalent or analogue thereof;

LRP2 HUMAN low-density lipoprotein receptor-related protein 2 precursor (megalin), including amino acids 4616- 4620 having the sequence SPSLP or a  
10 functional equivalent or analogue thereof;

IDD HUMAN integral membrane protein DGCR2/IDD precursor (KIAA0163), including amino acids 526- 530 having the sequence SGSTP or a functional  
15 equivalent or analogue thereof;

AMFR HUMAN autocrine motility factor receptor precursor (AMF receptor) (GP78), including amino acids 203- 207 having the sequence SVSPP or a functional equivalent or analogue thereof; and

20 ACH5 HUMAN neuronal acetylcholine receptor protein, alpha-5 chain precursor, including amino acids 382-386 having the sequence SGSGP or a functional equivalent or analogue thereof.

11. A binding motif according to claim 1 wherein at least one serine residue of  
25 the amino acid sequence is phosphorylated.

12. A binding motif according to claim 11 wherein a second serine residue from the 5' end of the motif is phosphorylated.

30 13. A binding motif according to claim 11 wherein the receptor is a GM-CSF/IL-3/IL-5 receptor capable of binding a cytoplasmic protein, said binding motif comprising an amino acid sequence including the sequence <sup>582</sup>HSRSLP<sup>587</sup> of the GM-CSF/IL-3/IL-5 receptor or a functional equivalent or analogue thereof wherein at least Ser<sup>585</sup> is capable of being phosphorylated.

14. A phosphorylated binding motif of a GM-CSF/IL-3/IL-5 receptor capable of binding a cytoplasmic protein, said binding motif comprising an amino acid sequence including the sequence <sup>582</sup>HSRSLP<sup>587</sup> of the GM-CSF/IL-3/IL-5  
5 receptor or a functional equivalent or analogue thereof wherein at least Ser<sup>585</sup> is phosphorylated.

15. A method of phosphorylating a binding motif of a receptor capable of binding a cytoplasmic protein, said binding motif comprising an amino acid  
10 sequence, a functional equivalent or analogue thereof and wherein at least one amino acid is serine, said method comprising binding a triggering molecule to the receptor.

16. A method according to claim 15 wherein the serine residue corresponds to  
15 a serine residue at position 585 of the common  $\beta_c$  according to Figure 1.

17. A method according to claim 15 wherein the triggering molecule corresponds to its receptor.

20 18. A method according to claim 17 wherein the triggering molecule is a cytokine which binds to its corresponding receptor.

19. A method according to claim 18 wherein the receptor is a GM-CSF/IL-5/IL-3 and the triggering molecule is selected from the group including GM-CSF, IL-5  
25 or IL-3.

20. A method of binding a cytoplasmic protein to a receptor, said method comprising:

30 phosphorylating a binding motif according to claim 1, a functional equivalent or analogue thereof; and

subjecting the binding motif of the receptor to a cytoplasmic protein.

21. A method of activating cellular activities said method including:

regulating the activation of phosphorylation of a binding motif of a receptor according to claim 1, a functional equivalent or analogue thereof; and

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subjecting the binding motif to a cytoplasmic protein wherein said cytoplasmic protein is associated with cellular activities.

22. A method of regulating cellular activities, said method including:

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regulating the phosphorylation of a binding motif of a receptor according to claim 1, a functional equivalent or analogue thereof;

subjecting the binding motif to a cytoplasmic protein to bind the cytoplasmic protein to the binding motif; and

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activating a cell signaling pathway by interacting the bound cytoplasmic protein with a signaling molecule involved in the pathway.

23. A method according to claim 20 wherein the cytoplasmic protein is 14-3-3 protein.

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24. A method according to claim 21 wherein the cellular activities or cell signalling pathways are selected from the group including cell survival, proliferation, transformation, differentiation, mitogenesis, chemotaxis, motility, enhanced phagocytosis, bacterial killing, superoxide production and cytotoxicity.

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25. A method according to claim 23 wherein the cell signaling pathway is the PI-3-kinase pathway.

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26. A method of inhibiting cell survival, said method including inhibiting the binding of a cytoplasmic protein to a binding motif of a receptor according to claim 1.

27. A method according to claim 26 wherein inhibition of the binding is via an antagonist which binds to the receptor motif, said antagonist selected from the



group including antibodies, small peptides, small molecules, peptide mimetics or any type of molecule known to those skilled in the art that are directed to the cytoplasmic binding motif so as to prevent attachment of cytoplasmic proteins to a phosphoserine residue or a signaling molecule.

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28. A method of inhibiting cell activation, said method including inhibiting the binding of a cytoplasmic protein to a binding motif of a receptor according to claim 1.

10 29. A method of treating a cytokine mediated condition said method comprising:

regulating the activation of phosphorylation of a binding motif of a receptor according to claim 1, a functional equivalent or analogue thereof.

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